UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,725	12/21/2001	Sabine Flicker	25401-4	9787

24256 7590 02/25/2004

DINSMORE & SHOHL, LLP
1900 CHEMED CENTER
255 EAST FIFTH STREET
CINCINNATI, OH 45202

EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,725	FLICKER ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/21/03; 6/11/02; 12/21/01*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 13-24* is/are pending in the application.

4a) Of the above claim(s) *21-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/11/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-8 and 13-24 are pending.

2. Applicant's election with traverse of Group I, Claims 1-20 (now claims 1-8 and 13-20) drawn to a Group 2 allergen specific human IgE Fab directed to clone 94 having the specific heavy chain amino acid sequence of SEQ ID NO: 7, encoded by the nucleic acid sequence of SEQ ID NO: 1 and the specific light chain amino acid sequence of SEQ ID NO: 10, filed 12/19/03, is acknowledged. The traversal is on the grounds that (1) it would not be unduly burdensome for the subject matter of each of the clones 60, 94 and 100 to be examined in the same application. (2) SEQ ID NO: 2, 5, **8** and 11 are directed to clone 60 and SEQ ID NO: 3, 6, 9 and 12 are directed to clone 100. Upon reconsideration, the group 2 allergen specific human IgE Fabs directed to clones 60 and 100 have been examined along with the elected clone 94 having the amino acid sequences 7-12. Therefore, the requirement of Group 1 (now claims 1-8 and 13-20) and Groups 2-4 is still deemed proper and is therefore made FINAL.

3. Claims 21-24 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-8 and 13-20 drawn to group 2 allergen specific human IgE Fab directed to clones 95, 60 and 100 having the amino acid sequences 7-12 are being acted upon in this Office Action.

5. Claims 1-3, and 13 are objected to for missing the article "A" for said independent claims.

6. Claims 4-5 and 14-15 are objected to for missing the article "The" for said dependent claims.

7. The disclosure is objected to for failing to comply with the requirements of 37 C.F.R. 1.821(d), specifically, SEQ ID NO is required for pages 17-20. Appropriate correction is required.

8. The disclosure is objected to because of the following informalities: (1) it is noted there is a discrepancy among the amino acid sequences among clones 60, and 94. The amendment filed 6/11/02 to the specification on page 8 and 10 indicates that the heavy chain amino acid sequence of **clone 94** is SEQ ID NO: **8**, while the heavy chain amino acid sequence for **clone 60** is SEQ ID NO: **7**. Further, it is not clear which light chain amino acid sequence (SEQ ID NOS: 10-12) goes with which clone. Assuming the heavy and light chain sequences and the corresponding clones as indicated by the election filed 2/19/03 is correct, the amendment to heavy and light chain sequences for the corresponding clones filed on 6/11/02 is incorrect. (2) "SEQUENCE LISTING ID NO 1A" on page 17 should have been "Table 2", (3) "SEQUENCE LISTING ID NO 1B" on page 18 should have been "Table 3", (4) "SEQUENCE LISTING ID NO 2A" on page 19 should have been "Table 4", (5) "SEQUENCE LISTING ID NO 2B" on page 19 should have been "Table 5" and (6) "Fabsas" on page 7, line 22 should have been "Fabs as". Appropriate action is required.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-8 and 13-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) three Phl p2 specific human IgE Fab fragments consisting of a heavy chain and a light chain wherein the heavy chain amino acid sequence consists of SEQ ID NO: 7 and the light chain amino acid sequence consists of SEQ ID NO: 10 or a heavy chain consisting of SEQ ID NO: 8 and a light chain consisting of SEQ ID NO: 11, or a heavy chain consisting of SEQ ID NO: 9 and a light chain consisting of SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, (2) An Phlp2 specific antibody comprising the variable region comprising a heavy chain, and a light chain and a human IgG wherein the heavy chain amino acid sequence is set forth in SEQ ID NO: 7 and the light chain amino acid sequence is set forth in SEQ ID NO: 10 or a heavy chain is set forth in SEQ ID NO: 8 and a light chain is set forth in SEQ ID NO: 11, or a heavy chain is set forth in SEQ ID NO: 9 and a light chain is set forth in SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, and (3) a diagnostic reagent or a kit comprising said Phl p2 specific human IgE Fabs and/or said specific Phl p2 antibody mentioned above for detection assay, **does**

not reasonably provide enablement for *any* group 2 allergen specific human IgE-Fabs having *any* combination of the amino acid sequence or "essentially homologous variant thereof" as set forth in claims 1, 4 and 5, *any* group 2 allergen specific human IgE-Fabs having *any* combination of nucleic acid sequence or "essentially homologous variant thereof" as set forth in claims 2, 13 and 14, *any* Group 2 allergen specific human IgG as set forth in claims 3 and 15 and any vaccine (claims 8, and 19) or diagnostic agent (claims 6, 16, and 17) or diagonistic kit (claims 7, 18 and 19) comprising any IgE-Fabs or any IgG mentioned above for treating any type I allergy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The breath of the claims encompasses human IgE Fab comprising any combination of heavy and light chain of human IgE Fab having the amino acid sequence of SEQ ID NO: 7-12 or any combination of nucleic acid sequence of SEQ ID NO: 1-6, any "essentially homologous variant" of the heavy and the light chains having the amino acid sequence of SEQ ID NO: 7-12, any homologous variant of the heavy and light chains encoded by the nucleic acid sequence of SEQ ID NO: 1-6, any human IgG comprising the combination of heavy and light chain of human IgE Fab having the amino acid sequence of SEQ ID NO: 7-12 or encoded by the nucleic acid sequence of SEQ ID NO: 1-6, any homologous variant of heavy and light chain having the amino acid sequence of SEQ ID NO: 7-12, or any homologous variant of heavy and light chain encoded by the nucleic acid sequence of SEQ ID NO: 1-6 for a vaccine.

The specification discloses only three Phl p2 specific human IgE Fab fragments consisting of a heavy chain and a light chain wherein the heavy chain amino acid sequence consists of SEQ ID NO: 7 and the light chain amino acid sequence consists of SEQ ID NO: 10 or a heavy chain consisting of SEQ ID NO: 8 and a light chain consisting of SEQ ID NO: 11, or a heavy chain consisting of SEQ ID NO: 9 and a light chain consisting of SEQ ID NO: 12 for

inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, (2) An Phlp2 specific antibody comprising the variable region comprising a heavy chain, and a light chain and a human IgG wherein the heavy chain amino acid sequence is set forth in SEQ ID NO: 7 and the light chain amino acid sequence is set forth in SEQ ID NO: 10 or a heavy chain is set forth in SEQ ID NO: 8 and a light chain is set forth in SEQ ID NO: 11, or a heavy chain is set forth in SEQ ID NO: 9 and a light chain is set forth in SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, and (3) a diagnostic reagent or a kit comprising said Phl p2 specific human IgE Fabs and/or said specific Phl p2 antibody mentioned above for detection assay (See pages 13 and 17-18). The specification further discloses all three IgE Fabs bound to the same recombinant fragment consisting of the N-terminal 64 amino acids of Phl p2. The specification discloses grafting the variable regions of the Phl p2 specific human IgE Fab fragments onto human IgG1 (page 3) for suppressing Phl p2 degranulation of basophiles.

The specification does not teach how to make and use *any* group 2 allergen specific human IgE Fab as set forth in claims 1-8 and 13-20 because there is insufficient guidance as to which amino acid sequence of the light chain from SEQ ID NO: 10-12 when combined with which heavy chain from SEQ ID NO: 7-9 or the corresponding nucleic acid sequence or any homologous variant thereof would maintain the same binding specificity as the Fab fragment from clone 94, 60 and 100. There is insufficient guidance as to which amino acid within the light chain and heavy chain of SEQ ID NO: 7-12 can be modified such as substitution, deletion, or addition and whether the resulting human IgE Fab would maintain the same binding specificity as the Phl 2 specific human IgE Fab of clone 94, 60 and 100. Likewise, there is insufficient guidance as to which nucleotide within the light chain and heavy chain as set forth in SEQ ID NO: 1-6 can be modified and whether the resulting human IgE Fab in which combination would maintain the same binding specificity as the Phl 2 specific human IgE Fab of clone 94, 60 and 100. Further, the term "having" is open-ended. It expands the amino acid sequence and the corresponding polynucleotide encoding the Fab fragment of clones 94, 60 and 100 to include additional amino acid residues at either end or the corresponding nucleotides at either or both ends. There is insufficient guidance in the specification as to which undisclosed amino acids or nucleotides to be included and whether the resulting modified human IgE Fab would still bind to Phl p2.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are

critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed "homologous variant" of human IgE Fab, it is unpredictable which undisclosed Phl p2 allergen specific human IgE Fab "homologous variant" of the amino acid sequences or the nucleic acid sequence would bind specifically to Phl p2, in turn would be useful for diagnosis, let alone a vaccine against type I allergy. Further, there is insufficient in vivo working demonstrating that the undisclosed human IgE Fab having any combination of amino acid sequence or nucleic acid sequence could inhibit the binding of grass pollen allergic patient IgE antibodies to Phl p2, in turn would be useful for inhibiting mast cell degranulation in vivo for use as a vaccine against type I allergy. The specification does not teach how to extrapolate data obtained from in vitro binding inhibition assays to the development of effective vaccine against type I allergy. It is not clear that the skilled artisan could predict the efficacy of the human IgE Fab having any combination of heavy and light chain, any undisclosed variants thereof and/or any human IgG constant region for a vaccine. Further, human allergen specific IgE having constant region may activate effector cells to release biologically active mediators via receptor crosslinking. A vaccine in the absence of in vivo working example are unpredictable because other functional properties, known or unknown, may make the antibody unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). Since the binding specificity of the human IgE Fab is not enabled, it follows that the complete antibody comprising the variable regions of said IgE Fabs and human IgG is not enable. It also follows that any IgE-Fabs directed against any Phl p2 or recombinantly produced is not enabled. It also follows that any diagonistic reagent, vaccine or kit comprising the undisclosed Group 2 allergen specific human IgE Fab or any Group 2 allergen specific human IgG mentioned above are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

11. Claims 1-8 and 13-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *any* group 2 allergen specific human IgE-Fabs having *any* combination of the amino acid sequence or "essentially homologous variant thereof" as set forth in claims 1, 4 and 5, *any* group 2 allergen specific human IgE-Fabs having *any* combination of nucleic acid sequence or "essentially homologous variant thereof" as set forth in claims 2, 13 and 14, any Group 2 allergen specific human IgG as set forth in claims 3 and 15 and any vaccine (claims 8, and 19) or diagnostic agent (claims 6, 16, and 17) or diagonistic kit (claims 7, 18 and 19) comprising any IgE-Fabs or any IgG mentioned above for treating any type I allergy.

The specification discloses only three Phl p2 specific human IgE Fab fragments consisting of a heavy chain and a light chain wherein the heavy chain amino acid sequence consists of SEQ ID NO: 7 and the light chain amino acid sequence consists of SEQ ID NO: 10 or a heavy chain consisting of SEQ ID NO: 8 and a light chain consisting of SEQ ID NO: 11, or a heavy chain consisting of SEQ ID NO: 9 and a light chain consisting of SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, (2) An Phlp2 specific antibody comprising the variable region comprising a heavy chain, and a light chain and a human IgG wherein the heavy chain amino acid sequence is set forth in SEQ ID NO: 7 and the light chain amino acid sequence is set forth in SEQ ID NO: 10 or a heavy chain is set forth in SEQ ID NO: 8 and a light chain is set forth in SEQ ID NO: 11, or a heavy chain is set forth in SEQ ID

NO: 9 and a light chain is set forth in SEQ ID NO: 12 for inhibiting the binding of grass pollen allergic patient's IgE to Phl 2 in vitro, and (3) a diagnostic reagent or a kit comprising said Phl p2 specific human IgE Fabs and/or said specific Phl p2 antibody mentioned above for detection assay (See pages 13 and 17-18). The specification further discloses all three IgE Fabs bound to the same recombinant fragment consisting of the N-terminal 64 amino acids of Phl p2. The specification discloses grafting the variable regions of the Phl p2 specific human IgE Fab fragments onto human IgG1 (page 3) for suppressing Phl p2 degranulation of basophiles.

With the exception of the three Phl p2 specific human IgE Fabs having the specific combination of heavy and light chain and the specific immunoglobulin comprising the variable region of the specific IgE Fab and human IgG1 for inhibiting the binding of grass pollen allergic patients IgE antibodies to Phl p2, there is insufficient written description about the binding specificity of any Group 2 allergen specific human IgE Fab comprising any combination of the amino acid sequence or nucleic acid sequence. Further, there is inadequate written description about the structure such as the amino acid sequence or the corresponding nucleotide sequence associated with function of *any* "homologous variant" of any Group 2 allergen specific human IgE Fab, let alone any vaccine, diagnostic agent, and kit comprising the undisclosed Group 2 allergen specific human IgE Fab or human IgG. There is inadequate written description about which amino acid within the light chain and heavy chain of SEQ ID NO: 7-12 or nucleic acid sequence as shown in SEQ IDNO: 1-6 can be modified such as substitution, deletion, or addition and whether the resulting human IgE Fab would maintain the same binding specificity as the Phl 2 specific human IgE Fab of clone 94, 60 and 100. Further, the term "having" is open-ended. It expands the amino acid sequence and the corresponding nucleotide sequence of the Fab fragment to include additional amino acid residues or nucleotides at either or both ends and whether the undisclosed human IgE Fab maintain its binding specificity as clones 94, 60 and 100, in turn, useful for diagnostic purpose. Since the binding specificity of the human IgE Fab is not adequately described, it follows that the complete antibody comprising the variable regions of said IgE Fabs and human IgG is not adequately described. It also follows that any IgE-Fabs directed against Phl p2 or recombinantly produced is not adequately described. It also follows that any diagnostic reagent, vaccine or kit comprising the undisclosed Group 2 allergen specific human IgE Fab or any Group 2 allergen specific human IgG mentioned above are not adequately described.

The specification discloses only three Phl p2 specific human IgE Fabs. Given the lack of a written description of *any* additional representative species of homologous variant as encompassed by the claims for a vaccine, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 1-2, 4-6, 8, 14, 16 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Steinberger *et al* (J Biol Chem 271(18): 10967-72, 1996; PTO 892).

Steinberger *et al* teach allergen specific human IgE Fab having the amino acid sequences homologous to the amino acid sequence of SEQ ID NO: 10 (See page 10970, Figure 5B, in particular) and SEQ ID NO: 7 (See page 10970, Figure 4, in particular). The reference recombinant human IgE Fab encoded by the nucleic acid sequence such as the ones in Figure 5A is a homologous variant of the claimed SEQ ID NO: 4. The term "essentially homologous variant" includes the reference heavy and light chain of the reference allergen specific human IgE Fab. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Claims 4 and 14 are included in this rejection because the reference antibody may crossreact with Phlp2 because of the homologous CDR1-3 in the light chain. Claim 6 is included in this rejection because the reference recombinant human IgE Fab is useful for diagnostic reagent in detection and competing with IgE binding to Phl p5 allergen in vitro. Claims 8 and 20 are included in this rejection because Steinberger *et al* teach the reference allergen specific human IgE Fab is useful as blocking antibodies for passive therapy in the

allergic effector organs (See page 10972, column 1, in particular). Thus, the reference teachings anticipate the claimed invention.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 2, 3, 13, 15, 16, 17, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinberger *et al* (J Biol Chem 271(18): 10967-72, 1996; PTO 892) in view of US Pat No 5,254,671A (Oct 1993; PTO 892).

The teachings of Steinberger *et al* have been discussed supra.

The claimed invention in claims 3, 13, and 15 differs from the teachings of the reference only that the allergen specific human IgE Fab comprising human IgG.

The claimed invention in claims 16, 17 and 20 differs from the teachings of the reference only that the diagnostic reagent comprising a complete antibody.

The '671 patent teaches various human IgG and a method of making said human IgG such as human IgG1 and IgG3 and the variable regions of IgE Fab (See column 12, line 26-42, in particular). The '671 patent further teaches that the antibodies having human IgG1 or IgG3 subclass are useful because they are less immunogenic and can mediate antibody mediated cellular cytotoxicity (ADCC) or complement mediated cellular lysis to down regulate or lysis B cells expressing IgE (See column 12, lines 46-57, in particular). The '671 patent teaches that the reference antibody is useful for in vivo therapy such as vaccine to treat IgE-mediated allergies in

humans (See column 15, lines 63-65, column 16, lines 31-37, in particular), and diagnostic use (column 17, lines 17, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the variable regions of the IgE Fab as taught by the '671 for the variable regions of the allergen specific human IgE having homologous amino acid sequence to the claimed SEQ ID NO: 7 and 10 or the nucleic acid encoding said homologous amino acid sequence as taught by Steinberger *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '671 patent teaches that antibodies having human IgG1 or IgG3 subclass are useful because they are less immunogenic and can mediate antibody mediated cellular cytotoxicity (ADCC) or complement mediated cellular lysis to down regulate or lysis B cells expressing IgE (See column 12, lines 46-57, in particular). Steinberger *et al* teach the reference allergen specific human IgE Fab is useful as blocking antibodies for passive therapy in the allergic effector organs (See page 10972, column 1, in particular).

17. Claims 1, 2, 6, 7, 16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinberger *et al* (J Biol Chem 271(18): 10967-72, 1996; PTO 892) in view of5,945,294A (Aug 1999; PTO 892).

The teachings of Steinberger *et al* have been discussed supra.

The claimed invention in claim 7 differs from the teachings of the reference only that a diagnostic kit comprising the an allergen specific human IgE Fab having the homologous amino acid sequence as shown in SEQ ID NO: 7 and 10.

The claimed invention in claim 18 differs from the teachings of the reference only that a diagnostic kit comprising the an allergen specific human IgE Fab encoded by the essentially homologous variant of SEQ ID NO: 1 and 4.

The '294 patent teaches diagnostic kit for IgE detection using human Fc epsilon receptor (See abstract, in particular). The kit is useful for diagnosing abnormal conditions in animals that are associated with changing levels of IgE associated with allergy (See column 15, lines 19-23, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to put the antibody taught by Steinberger *et al* in a kit as taught by the '294 for diagnostic assays. One would have been motivated, with a reasonable expectation of success to do this for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '294 (See column 14, in particular). From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

18. Claims 17, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinberger *et al* (J Biol Chem 271(18): 10967-72, 1996; PTO 892) in view of US Pat No 5,254,671A (Oct 1993; PTO 892) as applied to claims 1, 2, 3, 13, 15, 16, 17, and 20 and further in view of US Pat No 5,945,294 (Aug 1999, PTO 892).

The combined teachings of Steinberger *et al* have been discussed supra.

The claimed invention in claims 17 and 19 differs from the combined teachings of the references only that a diagnostic kit comprising the an allergen specific human IgG comprising the variable regions of the allergen specific human IgE having the homologous amino acid sequence as shown in SEQ ID NO: 7 and 10 or complete antibody.

The claimed invention in claim 18 differs from the combined teachings of the references only that a diagnostic kit comprising the allergen specific complete antibody.

The '294 patent teaches diagnostic kit for IgE detection using human Fc epsilon receptor (See abstract, in particular). The kit is useful for diagnosing abnormal conditions in animals that are associated with changing levels of IgE associated with allergy (See column 15, lines 19-23, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to put the allergen specific complete antibody such as human IgG comprising the variable regions of the allergen specific human IgE having the homologous amino acid sequence as shown in SEQ ID NO: 7 and 10 as taught by Steinberger *et al* and the '671 patent in a kit taught by the '294 for diagnostic assays. One would have been motivated, with a reasonable expectation of success to do this for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '294 (See column 14, in particular). From

the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

21. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
February 23, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600